

# Effects of Breastfeeding, Maternal BMI, Gestational Age, and Birth Weight on Adiposity Rebound

Octavia Foster and Nicole Stendell-Hollis

Central Washington University

## ABSTRACT

**Background:** Adiposity rebound (AR) is defined as the age in which children exhibit a nadir in body mass index (BMI)-for-age and begin to exhibit an increase from that nadir. The purpose of this project is to perform a literature review of factors that influence timing of AR in children.

**Methods:** This review of literature research investigation utilized a two-step search methodology. Research articles were identified utilizing electronic databases including PubMed, google scholar, Academic search complete, among other databases.

**Results:** Investigations for the factors, breastfeeding, maternal BMI, infant gestational age, and infant birth weight, exhibited mixed results. Investigations typically identify the association that having a healthy BMI prior to pregnancy has beneficial impact on AR timing.

**Conclusions:** The mixed results observed appear to be influenced by ethnicity and geographical location. Therefore, decisions on maximizing the health and delaying AR timing of the infant must occur in an individualized setting between the mother and/or parents and healthcare provider.

## Introduction

Adiposity rebound (AR) is defined as the age in which children exhibit a nadir in body mass index (BMI)-for-age and begin to exhibit an increase from that nadir.<sup>1</sup> In U.S. children this typically occurs between 5-7 years of age.<sup>1</sup> AR is typically considered premature if it occurs between 5-5.5 years of age.<sup>2</sup> Although premature AR is associated with a plethora of non-communicable, preventable diseases, the most notable association is between obesity and premature AR.<sup>2</sup> Between 1999-2000 U.S. adult obesity incidence was 30.5%; 2017-2018 data on this population indicated a rise in incidence of 11.9% increasing the obesity incidence rate to 42.4%.<sup>3</sup> The trend of increasing obesity rates between generations is also mirrored in children. In 1999-2000 childhood, ages 2-19, obesity incidence was 13.9%; 2017-2018 data indicates obesity incidence rose to 19.3% for children.<sup>4</sup>

Apart from the associations between obesity and the development of co-morbidities, increased obesity rates are also associated with an increase in obesity-related medical spending cost. In the U.S. in 2012 21% of medical spending was due to the treatment of obesity related morbidities.<sup>5</sup> Some research suggest that U.S. obesity related medical cost may rise to \$48-\$66 billion per year if obesity interventions are not implemented effectively.<sup>6</sup> It is important to note however that it is difficult to compare obesity-related medical spending between different countries; each country individually defines what aspects of medical treatment are considered obesity related. With increased research indicating the association between obesity and premature AR it is critical to investigate factors that postpone AR in order to attenuate the risk of obesity and obesity-related morbidity incidence.

Additionally, quality of life is significantly diminished for both children and adults suffering from obesity and its associated chronic illnesses.<sup>7</sup> Socio-cultural constructs have perpetuated an environment of obese shaming resulting in social inequalities such as bullying and stigma regarding their weight which often afflicts children more significantly.<sup>7</sup> Childhood obesity that is not attenuated is associated with increased severity of obesity in adulthood

and obesity related morbidities when compared to individuals that become obese in adulthood but were of normal weight in childhood.<sup>7</sup>

AR timing in obese individuals not only impacts their offspring but many generations thereafter.<sup>8</sup> Both genetic and socio-cultural factors of obese individuals suggest that their children and generations thereafter will develop obesity at some point in their lifetime.<sup>8</sup> Premature AR also has significant correlations with the development of insulin resistance, cardiovascular disease, high cholesterol, high blood pressure, and a host of other metabolic conditions including polycystic ovarian syndrome.<sup>2</sup> As childhood obesity rates continue to rise the average age of AR has significantly decreased. Although the relationship between AR and obesity is well studied, there is not sufficient data available to decipher what factors influence AR leaving a gap in knowledge. Therefore, research investigating what factors affect AR timing warrants further study. Determining which factors most strongly influence AR may aid in implementing funding, services, and policy to maximize protective effects against obesity and obesity-related comorbidities for generations to come while also decreasing the exuberant medical spending for obesity-related conditions. However, it is critical that these investigations occur globally and in various ethnically diverse regions of countries as sociocultural environments may alter the impact of specific AR factors.

Existing research suggests that the following factors influence AR timing. Research on the association of breastfeeding (BF) and AR timing suggest that only the upper quantiles of normal BMI distribution are shifted; this indicates confounding factors may limit the effects of BF on the entire BMI distribution.<sup>9</sup> Multiple studies suggest that maternal BMI is the strongest indicator of early AR (EAR).<sup>10-12</sup> Research indicates that preterm infants are at an increased risk of EAR except for those considered U.S. citizens; this suggests confounding factors may negate the association between AR timing and GA in U.S. infants.<sup>13,14</sup> Research on the association between small for gestational age (SGA) and AR timing indicates that infants 34<sup>3</sup> but <37 weeks exhibit EAR.<sup>15</sup>

The aim of this research is to investigate the influence on AR timing of four factors: 1) BF; 2) maternal BMI; 3) infant gestational age (GA); and 4) infant birth weight.

## Methods

### Search Strategy

This review of literature research investigation utilized a two-step search methodology. Jermaine research articles were identified utilizing electronic databases including PubMed, google scholar, Academic search complete, and other databases found by utilizing Central Washington University's research guides based on the keyword nutrition. Key search terms used to sequester research articles included different combinations of 'AR', 'obesity', 'breast-feeding', 'maternal weight', 'birthweight', 'SGA', 'GA', and 'maternal diet quality'. Data restrictions were not utilized for inclusion/exclusion criteria. This review of literature includes a total of 18 studies. The snowball method was utilized to identify additional prevalent publications; the reference lists of identified and acceptable articles were screened to identify supplementary relevant publications. Article identification for both stages was conducted and screened by thoroughly reading them and summarizing them in table format.

### Study Design

Studies included in this review of literature were comprised of non-randomized investigations; it is a clear ethical violation to randomize pregnant women and ultimately their unborn children to specific exposures that may elicit adverse outcomes of interest. Descriptive information regarding the included studies in the review of literature were extracted and summarized in table format. Information extracted included: (1) number of articles; (2) article DOI or other identification number; (3) author; (4) publication year; (5) design; (6) population; (7) results; (8) study type; (9) geographical origin; (10) risk of bias; and (11) funding source. The Assessment of Multiple Systemic Reviews,

AMSTAR, checklist was utilized in the methodological development phase of this investigation and during the writing process of this review of literature to maximize validity; the AMSTAR instrument evaluation was not an appropriate tool to evaluate the validity of the sources included in this investigation as the publications did not include randomized control trials but rather epidemiological studies. Included publications were limited to English publications or available English translated studies. This study was deemed exempt of Institutional Review Board approval..2

**Inclusion/Exclusion Criteria**

All studies were screened based on the following criteria: 1) the article describes self-conducted research; 2) maternal populations were low risk for adverse birth outcomes; 3) investigated one of the factors of interest; mother’s gestational BMI, gestational age, BF duration and/or incidence, or infants birth weight and its association with AR; 4) provided clear definitions and parameters for factors; i.e. obesity, small for gestational age, breastfed, etc.; 5) collected quantitative data; (6) provided a thoroughly developed methods section; (7) identified data sources; (8) identified funding sources; (9) the full article was accessible for free or provided for free through interlibrary loan; and (10) was published in English, or an English translation was available at time of selection.

All studies were screened and excluded from this review if any of the following criteria applied; : 1) the research included high risk obstetric populations; 2) the article summarized findings of other articles such as literature reviews or debates; 3) the main topic of research was not congruent with the factors of interest of this investigation and AR; 4) the researchers did not define clear definitions or parameters for investigated factors; 5) Publication authors indicated and/or the authors of this investigation perceived that funding sources posed any conflicts of interest with the research findings; (6) failed to provide a developed methods section; (7) the full article was not available for free via public databases and/or interlibrary loan; and (8) publications were not published in English or an English translation did not exist.

**Results**

**Table 1** summarizes literature describing the influence of BF on AR. BF is one of the factors that is most investigated for its association with delaying AR with much, but not all, of recent research supporting this association.

<b>Table 1. Summary of Breastfeeding Sources.</b>				
<b>Author</b>	<b>Methods</b>	<b>Subjects</b>	<b>Results</b>	<b>Conclusions</b>
Goh, et al 2022	This longitudinal study includes data from a screening program for infants (SPIC) provided by NHIS. Children were tracked from 4 – 71 months during seven time periods. Data collection included: anthropometric measurements, nutritional measurements, and other environmental parameters.	Korean infants (N=142,668) and their families who participated in the SPIC program.	Time period: <ul style="list-style-type: none"> <li>1 (4-6mos): formula feeding instead of BF increased risk of EAR in girls but not boys (23%; p=0.0009)</li> <li>2 (12mos): Feeding soy milk and cow’s milk increased risk of EAR compared to BF (47%; p=0.021, and 51%; p=0.0009; respectively).</li> </ul>	BF decreases the risk of EAR in girls in time period 1 and both boys and girls in time period 2.

Estrevez-Gonzalez, et al 2005	This retrospective study collected data from medical records of the Infantile Health Program of the Canarian Health Services of Gran Canaria. Data collected included: anthropometric data, type of feeding (formula or BF), and time of AR.	Children (N=1812) born in 2004 in Gran Canaria whose anthropometric data was collected at least once before age 4yrs and 8yrs.	Exclusive BF for the first 6mos of life did not delay EAR. Age of AR was 3.61 and 3.64 for formula and BFg, respectively.	No association was observed between exclusive BFg for the first 6mos of life and delay of EAR.
Wu, et al 2020	This longitudinal cohort study collected data from the Avon Longitudinal Study of Parents and Children (ALSPAC) study. Data collection included: anthropometric, type of feeding, and feeding behaviors. Genetic risk scores (GRS) were also evaluated.	Children (N=5266) born in Avon, UK between 4/1991 – 12/1992 were followed for over two decades.	GRS was negatively associated with timing of AR for both boys and girls. As GRS increased, so was the delay of AR in both boys and girls. Additionally, exclusive BFg for a minimum of 5mos delayed AR in girls, but not boys.	Exclusive BFg for a minimum of 5mos delayed AR in girls, and continued exclusive BFg delayed AR further; this was not observed in boys.
Chivers, et al 2010	This longitudinal cohort study collected data from the Raine study which followed children from birth through 14yrs. Anthropometric data and early infant feeding data were collected.	This study included 729 males and 674 females who participated in the western Australia Raine study.	Exclusive BFg for longer than 4mos was protective against EAR (p<0.001).	The results of this study found that exclusive BFg for at least 4mos was protective against EAR.

The literature summarizing the influence of maternal BMI on AR is depicted in **Table 2**. Much of the research indicated that maternal obesity prior or during early pregnancy is the most significant ante- or post-natal factor that influences AR timing.

Author	Methods	Subjects	Results	Conclusions
Linares, et al 2016	This longitudinal cohort study used data collected from the Growth and Obesity Chilean Cohort study. Data collection included pre- and post-pregnancy weight, pregnancy weight gain, and the timing of AR.	Mothers (N=594) who did not have gestational diabetes or were underweight were included.	Gestational weight gain was unrelated to AR timing. Elevated pre-pregnancy BMI and parity were significantly associated with early AR (OR=1.07; 95%CI=1.02-1.11; and OR=0.86; 95%CI=0.74-0.99, respectively).	Effective methods are needed to promote healthy pre-pregnancy BMI to prevent/delay early AR.
Doi, et al 2016	Prospective cohort study using data from the	Infants (N=2857) born	Maternal obesity (OR =2.89; 95%CI:2.09, 3.98)	The authors concluded that

	Growing up in Scotland cohort study. Annual anthropometric data was collected, as well as data regarding the timing of AR.	between 2004-2005 were included.	was found to be significantly associated with increased odds of obesogenic growth trajectory relative to no change trajectory.	maternal weight status was the strongest factor associated with EAR.
Roche, et al 2020	This longitudinal observational study collected anthropometric data and timing of AR in waves – Wave 1: 3-5yrs, and Wave 2: 6-8yrs.	Children born in France between January 1, 2003 and May 1, 2005 were included. Wave 1 consisted of 1159 children and Wave 2 consisted of 921 children.	Risk factors for overweight/obesity at ages 6-8yrs was associated with prenatal smoking (OR=3.0; 95%CI: 1.82, 4.95) and maternal and paternal obesity. These risk factors were decreased by BFG.	Tools need to be developed to identify those children who are at risk of overweight/obesity by 6-8yrs.
Giles, et al 2015	This prospective birth cohort study collected data to create predictive growth trajectories.	Australian children between 0-3.5yrs were followed until the age of 9.	Four distinctive growth trajectories were identified up to age 3.5: low, intermediate, high, and accelerating growth. Infants who fell into the high or accelerating growth trajectory were associated with increased BMI by age 9. Maternal obesity in early pregnancy was also associated with increased risk.	Maternal obesity was the strongest predictor of being in the accelerated group and having a higher BMI by age 9.
Cisse, et al 2021	Anthropometric and SNP markers data were collected from women and their offspring who participated in the Eden birth cohort study.	Pregnant French women (N=1415) who were pregnant between 2002-2006 and their offspring were included.	Maternal and paternal BMI, along with higher gestational weight gain, and smoking during pregnancy were associated with EAR.	Genetic SNP markers for obesity, parental BMI, and perinatal factors are associated with EAR.
Jacota, et al 2017	This study analyzed data from the Eden birth cohort study. Anthropometric data from mother-child pairs was collected.	Pregnant French women (N=1069) who were pregnant between 2003-2006 and their offspring were included.	When maternal age and education level were controlled for there was no significant association between maternal weight history and AR.	No association between BMI at age 5 and maternal and perinatal factors was observed for mothers who exhibited a normal pre-pregnancy BMI.

Ip, et al 2017	Dietary data and physical activity patterns were analyzed from a 2-year longitudinal study.	Latino Farm-worker children (N=248) between the ages of 2.5-3.5yrs and living in North Carolina were included.	Forty-one children (18.2%) had very EAR and 90 children (40%) had EAR. The remaining children were considered to non-rebounders (26.2%) or had non-classifiable growth curves (15.5%). Higher maternal BMI, and higher caloric intake was associated with EAR.	Approximately 60% of the children exhibited EAR. Higher levels of physical activity was associated with delayed AR.
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**Table 3** summarizes literature describing the influence of GA on AR. The impact of the length of gestational period had varying effect on AR and AR timing.

<b>Table 3. Summary of Gestational Age Sources.</b>				
<b>Author</b>	<b>Methods</b>	<b>Subjects</b>	<b>Results</b>	<b>Conclusions</b>
Franchetti, et al 2014	This study utilized data from the 21 <sup>st</sup> Century Longitudinal Survey in Newborns. This study collected demographic and anthropometric data from infants born in January 10-17, 2001 and July 10-17, 2001 at 6mos, 1.5, 2.5, 3.5, 4.5, and 5.5yrs.	Japanese female and male children (N=45,392) whose parents completed all surveys.	Obese children (39.6%) experienced EAR as early as 4.5yrs. The length of the gestational period was the most important factor influencing BMI and AR.	EAR occurs earlier in obese children compared to normal weight children.
Vereen et al 2019	This retrospective longitudinal study used anthropometric data collected from children born at U.S. military base in 2008.	Preterm (N=501) and full term (N=1423) born at a U.S. military base.	An EAR was associated with a higher BMI by age 8-9yrs, but was not related to gestational age. Early rapid catch-up growth was associated with EAR.	There was no association between gestational age and the timing of AR.
Baldassare, et al 2020	This prospective population-based longitudinal study utilized anthropometric data from infants born in 2009-2011.	Italian children (N=100) born at an intensive care unit in Bari, Italy.	EAR was identified in 54% of pre-term infants and in 30% of full-term infants. A significant association between gestational age and EAR was not observed. Breastfeeding duration and timing of introduction of solid foods were also not associated with EAR.	Premature birth may be a risk factor for EAR.

The literature summarizing the influence of infant birthweight on AR is shown in **Table 4**. Both small for gestational age and large for gestational age children generally had higher AR when compared to average gestational age children but this result was mixed.

**Table 4. Summary of Infant Birthweight Sources.**

Author	Methods	Subjects	Results	Conclusions
Shi, et al 2018	This longitudinal cohort study collected anonymous anthropometric data from SGA infants.	SGA infants (N=3004) born to term between August 2004-July 2010 in Shanghai, China.	Earlier AR and higher BMI at AR was observed for infants who displayed excessively rapid catch-up growth and rapid catch-up growth. Infants who crossed two percentiles in the first several months that were then adjusted to maintain average growth were less likely to exhibit adverse health outcomes.	Varying catch up growth patterns may pose increased or decreased risk of EAR.
Lin, et al 2021	The study collected data from a population based longitudinal study. Data collection included anthropometric data extracted from children's well visit records.	Children (N=13,616) born in Shanghai, China between September 2010-October 2013.	Sex, preterm birth, low birth weight, SGA, multiplet, and greater sleep duration was associated with significant differences in AR timing. Children who were born to advanced-age mothers and who were born SGA had a higher risk of EAR.	Timing of AR was associated with multiple risk factors. The protective effects of BFG on AR timing was not observed in durations longer than six months.
Maeyama, et al 2016	This longitudinal cohort study collected anthropometric data on infants at 4 and 9mos, and 1.5 and 3yrs.	Children (N=29,287) born in Kobe, Japan between 22-41wks gestation and complete medical records from birth to age 3yrs were included.	The BMI trajectory during the first 3 years was also GA-dependent, with a change in GA dependency at a boundary of 37 weeks GA. Approximately 7% of SGA children had already developed AR before 3 years of age.	Growth patterns during infancy and early childhood in SGA children differ depending on GA.
Joubert, et al 2013	This study included data from the Hungarian Longitudinal Growth Study. Anthropometric data was included in 2% of the sample size born between 1980-1983.	Hungarian children (N=1448) born between 1980-1983.	SGA and LGA infants had significantly higher risk of EAR compared to AGA infants.	The higher the intrauterine growth rate was observed was associated with higher BMI after birth and AR.

## Discussion

### Breastfeeding

BF is one of the factors that is most investigated for its association with delaying AR. Although much of recent research further supports this association some investigations have not identified delayed AR as an effect of BF.

Estrevéz-Gonzalez et. al (2015)<sup>16</sup> did not identify an association between BF and delayed AR. This retrospective cohort study utilized a subject pool of children born in 2004 in Gran Canaria. Researchers extracted information from medical records from the Infantile Health Program of the Carnarian Health Services of Grand Canaria. Breastfed children (N=173) and non-breastfed children (N=192) were included in the analysis. Collected data included weight and height measurements for the purpose of calculating BMI to estimate age at AR for all included subjects in analysis I. In analysis II, AR and percentages of weight groups, normal, overweight, and obese, were compared between the breastfed and non-breastfed groups. The result of this analysis suggests that exclusive BF for the first six months of life did not delay AR. The data suggest that age of AR was 3.61 and 3.64 for formula and breastfed groups, respectively. Although this data is not congruent with other research, Estrevéz-Gonzalez et. al indicates that this may be due to a lack of global consensus on the age of AR; 5-7years, 4-8 years, and 3-7 years have all been utilized as appropriate time frames for AR to occur in research. This lack of consensus indicates subjects exhibit EAR irrespective of feeding method for the 5-7 years and 4-8 years ranges, when utilizing the range 3-7 years children exhibited appropriate AR despite feeding method. The researchers also articulated that AR is exhibited earlier in this study than is typically reported in other literature, however, this population also exhibit higher rates of obesity than others; 18.3% nationally. Congruent with other research the data suggest that EAR or AR timing differs between genders. The researchers ultimately acknowledge that their results are atypical and suggest that these results warrant further research given the results of previous investigations. The authors also indicate that although their data does not reflect this, it is possible that extended BF may delay AR and that the association simply was not observed in this population.

A longitudinal cohort investigation by Chivers et. al in 2010<sup>17</sup> utilizing data from the Raine Cohort also elicited mixed results in terms of BF's association with delayed AR. This investigation included a total of 729 males and 674 females from Western Australia. During the original data collection of the Raine cohort study, anthropometric data was collected at birth, one, two, three, four, six, eight, ten, and 14 years of age. Multiple pregnancies, infants with congenital abnormalities, and preterm births were excluded from subject data inclusion. All anthropometric data was collected by trained staff using strict measurement protocols. Parental recall to specific interview questions were used to collect data on early infant feeding methods at the follow up visits at one, two, and three years of age; maternal figures specifically were asked to report age when BF stopped, age when regular milk was introduced, and milk type included in infant formula. In addition to information collected during the interviews, the mother's diary of early feeding milestones was utilized in conjunction to determine feeding method as well as to verify answers to other questions asked during the interview process. Due to the measurement schedule in the original Raine cohort study a gap in the data exist from 4-5.5 years of age; this data gap includes the timing range for both EAR and normal AR. The authors also indicate that a slight selection bias may also impact the results of this analysis; individuals were typically from higher socioeconomic status families with mothers older than 20 years compared to subjects that were not included in the sample.

This research indicates there was a significant negative association between age at which BF was stopped and weight group at 14 years of age;  $P<.001$ . A significant difference was observed between age at AR and weight status groups as well for a subset of 171 subjects;  $P<.010$ . However, the data indicates that there is no association between age at BF termination or age at introduction of other milk with AR timing. Nonetheless, statistically significant differences between age at termination of BF or age at introduction of other milks was only identified in a mixed model that adjusted for age, gestational age, gender, and weight status;  $P=.005$ . This same mixed model also indicated that BMI at AR, irrespective of timing, was higher in subjects that stopped BF prior to or equal to four months of age;  $P=.003$ . This effect was also mirrored in subjects who received other milk equal or prior to four months of age based



on the mixed model;  $P=.002$ . Although these effects were only significant in a mixed model analysis controlling for other variables, the researchers conclude that exclusive BF for more than four months is protective against EAR and increased BMI at AR.

Wu et. Al (2020)<sup>18</sup> conducted a longitudinal study from the Avon Longitudinal Study of Parents and Children, ALSPAC, cohort study utilizing subjects based in Avon, U.K. Participants of the original cohort included pregnant women and their offspring of the pregnancy that resided in Avon, UK with delivery dates between April 1, 1991 through December 31, 1992; the children from these pregnancies were followed for over two decades for data collection. All 14,541 pregnancies included in the ALSPAC cohort study, along with an additional 542 pregnancies that were not included in the study but had available information, were invited to participate in the current longitudinal study. A total of 5266 children were included in the current study after exclusion criteria were analyzed throughout the subject pool. All anthropometric data was transposed from the ALSPAC cohort study which retrieve the data from medical records from birth to five years; this is the standard practice of healthcare in the UK. Data on infant feeding practices was collected from the mother's diary of early feeding milestones, an interview with the study nurse at the six-month follow up, and a survey questionnaire at the 15 month follow up. The original cohort study also calculated genetic risk scores (GRS) for obesity by evaluating 69 single nucleotide polymorphisms (SNPs) that are known to be related to Genetic Investigation of Anthropometric Traits as well as 25 independent, non-overlapping SNPs associated with pediatric BMI trajectories for a total of 94 SNPs.

The data from this investigation indicates that GRS was negatively associated with AR timing irrespective of gender. An increased GRS is associated with EAR; a GRS score of 5 compared to 2.5 delayed the age at AR by .36 years; 95% CI, .37-.46,  $p<.0001$ . Ultimately, the data suggest that as GRS increases AR delay also increases irrespective of gender. In terms of BF, the data indicates that exclusive BF for a minimum of five months delays AR in girls at all GRS levels; this association was observed in males, but it was not significant. The researchers ultimately conclude that exclusive BF for a minimum of five months delays AR and both girls and boys. Additionally, there appears to be a dosage effect of continued exclusive BF past five months. However, the authors articulate that the biological mechanisms regarding the protective effect of BF are not well understood; however, it may be the result of the micro-nutrient content or bioactive composition and nature of breastmilk.

More recent research by Goh et. al (2022)<sup>19</sup> further supports that BF has a protective effect on obesity by delaying AR in Korean infants. This longitudinal study includes data from a screening program for infants (SPIC) provided by the National Health Insurance Service, NHIS. Subjects were evaluated for anthropometric measures during seven-time periods; 4–6 months, 9–12 months, 18–24 months, 30–36 months, 42–48 months, 54–60 months, and 66–71 months as well as at birth by SPIC staff. Along with anthropometric data measurements of height and weight, data on nutritional measurements and other environmental parameters were also collected. Parents also completed questionnaires by NHIS regarding infant feeding practices.

During time-period I, 4–6 months, formula feeding increased the risk of EAR in girls but not boys by 23% when compared to breastfed infants;  $P=.009$ . Additionally, the data suggest that combining feeding methods, BF along with formula supplementation, exhibited a 14% increase the risk of EAR with  $P=.076$ . However, this association is not significant therefore utilizing a combination feeding method does not increase the risk of EAR. During time-period II, 9-12 months, the data suggests the introduction of soy milk increases the risk of EAR by 47% compared to BF;  $P=.021$ . This phenomenon is mirrored with the introduction of cow's milk as well with a 51% increased risk of EAR compared to BF;  $P=.009$ . Thus, the data indicates that BF decreases the risk of EAR in girls during time-period I and for both genders during time period II.

## Maternal BMI

Inappropriate maternal gestational weight gain is often associated with adverse health outcomes for the infant. However, research typically focuses on the impacts of maternal BMI, both prior and during pregnancy, on the timing of AR.

Giles et. al (2015)<sup>11</sup> analyzed data from the Australian Perspective Birth Cohort study to analyze the associations between maternal BMI before as well as during pregnancy and AR timing. The authors created growth trajectories from birth to 3.5 years using latent class growth models. Post and anti-natal predictors of growth trajectory were analyzed using multivariable logistic regression models; multivariable linear as well as logistic regression models were computed to determine the existence and/or direction of association between growth trajectory groups and BMI at age nine.

The researchers identified four distinct growth trajectories up to the age of 3.5; low, intermediate, high, and accelerating growth. BMI at age nine was associated with increased growth trajectory; the high and accelerated trajectory subjects exhibited an increased BMI compared to intermediate or low groups. This research indicated that maternal obesity prior or during early pregnancy is the most significant ante- or post-natal factor that influences AR timing. Maternal obesity during these critical time periods was associated with a 4X increased risk of being in the accelerated group which is associated with increased BMI. The authors discuss the importance of investing public funds into measures that prevent childhood obesity and obesity during a woman's reproductive years; the data indicates maternal obesity is the highest risk factor of demonstrating an association with EAR by increasing the risk of children belonging to the accelerated growth group.

Linares et. al (2016)<sup>20</sup> utilized data from 594 Chilean mothers and their children from the longitudinal growth and obesity Chilean cohort study to analyze the relationship between gestational BMI and AR. The data relied on maternal self-reported pre- and post-pregnancy weights; their height anthropometric data was measured and not self-reported. Subjects were separated into classifications based on BMI categories, normal weight, overweight, and obese. Weights of the offspring were measured from 4–6 years; BMI curves from 0–7 years or utilized to estimate AR with the data transcribed from health records from 0–3 years. The researchers categorize the children based on timing of AR; <5 years EAR, 5-7 years intermediate AR, and >7 years late AR. Logistical regression models were utilized to evaluate any associations between BMI, gestational weight gain, and AR. Mothers who exhibited diabetes or who were underweight were excluded from data inclusion in the investigation by Linares et. al.

The data from this investigation suggests that gestational weight gain was not associated with AR timing. However, the data indicates that pre-pregnancy BMI was associated with EAR; OR = 1.07, 95% CI= 1.02-1.11. The data also suggest that parity has a significant association with EAR; OR=0.86; 95% CI= 0.74-0.99. The subject classification results indicate that 33% of mothers were overweight pre-pregnancy, 31.2% exhibited gestational weight gain above the recommended threshold by the institute of medicine, and 45% of offspring exhibited EAR. The authors conclude that measures should be put in place to promote pre-pregnancy healthy BMI to inhibit or attenuate the incidence of EAR. The authors emphasize the importance of targeting first time mother populations to impact the incidence of EAR most effectively by way of influencing pre-pregnancy BMI.

Doi et. al (2016)<sup>12</sup> utilized data from birth cohort one of the growing up in Scotland cohort study. This study includes data from children who were born from 2004–2005; only one child per household was allowed to participate in the study. They were followed annually for the first six years of life, at which point follow-ups were biannually. Anthropometric data were collected in their home and BMI measurements were converted into percentiles based on a population reference in the UK in 1990. Children were categorized according to these BMI measurement into underweight, healthy weight, overweight, obese, second, 85<sup>th</sup>, and 95<sup>th</sup> percentile cut off points. The researchers conducted logistics regression to explore the associations between AR timing and obesogenic effects.

The data indicates that 67.4% of the children included in the study did not change weight categories in between measurement periods for the duration of the investigation. Additionally, 2/3 of the subjects exhibited normal growth pattern; the medium BMI percentile of the participants was the 70<sup>th</sup> percentile when utilizing the 1990 UK reference range. This shift in BMI percentile of the participant population suggests that there has been an overall shift in the BMI distribution of the general population of children born in Scotland; the data exhibit many of the children remaining in the same weight groups throughout the investigation. The data indicates that more factors are associated with changes in weight categories than in changes in BMI percentile. However, the data indicates that the strongest association with a higher BMI percentile in the offspring was maternal weight status during pregnancy. Therefore, the

authors concluded that prevention strategies to target EAR must target factors that occur before AR; maternal weight was the most significant factor in obesity incidents in offspring according to this data.

Roche et. al (2020)<sup>21</sup> conducted a longitudinal observational study which included subjects born in France between January 1, 2003 – May 1, 2005. In the study two waves of evaluations were performed, wave I was conducted from 3–5 years, and the wave II was conducted from 6–8 years. Data was collected from 1159 French children who participated in wave I; these children attended public and/or private schools and participated in the school's annual medical exams. Ante- and post-natal data was transcribed from school health records as well as collected via parental interviews. Anthropometric measures done during the school's annual health exams were conducted by nurses from the protection of mother and infant service. Wave I data collection occurred from March – July 2008 while wave II data collection was conducted from March – July 2011; 921 children completed wave II out of the 1159 children who completed wave I. Subjects were classified based on BMI, BMI z-score for age and sex, and gestational age at birth. EAR was classified as earlier than 5.5 years; this was evaluated using a double-blind method by two of the authors using BMI z-scores and French curves. Chi-squared or fishers exact test, students T test, or ANOVA depending on the variable was utilized to evaluate associations between the factors and AR timing; two unique types of EAR were identified.

The bivariate analysis of the data suggests that risk factors for developing overweight/obesity in children at the age of 6–8 is associated with exposure to prenatal smoking, maternal obesity, paternal overweight/obesity, and catch-up growth; maternal overweight OR 3.00; 95 % CI 1.82, 4.95. The data indicates that factors that decrease the development of overweight/obesity at age 6–8 years include BF for at least six months compared to formula feeding; OR 0.42; 95 % CI 0.21, 0.84. 40.4% of children exhibited early AR; 26.3% of children in this category developed overweight/obesity at 6-8 years. Those with type A-EAR developed overweight/obesity at 6-8 years; those with type B-EAR did not. Type A-EAR occurs when there is an increase of at least 0.5 units in BMI z-score between the starting point of the AR and the last point if BMI is above the median z-score; there is an increase equal to or greater than 1 unit in BMI z-score between the starting point of the AR and the last point if BMI is below the median. Type B-EAR is defined as there is an increase greater than 0.5 but lower than 1 unit in BMI z-score between the starting point of the AR and the last point if the BMI is below the median. Based on the data the authors suggest that a more precise EAR screening tool needs to be developed and implemented to effectively aim resources at those at the most risk of developing obesity later in life. Type A- EAR children exhibited overweight/obesity by 6–8 years while type B-EAR children did not. Therefore, tools need to be developed to differentiate and identify type A-EAR children from type B-EAR children in order to prevent the development of obesity-related diseases.

Cisse et. al (2021)<sup>22</sup> utilized the Eden birth prospective cohort study for a data source for this investigation. The Eden cohort study included 1415 French, Caucasian, pregnant women, and their children before 24 weeks gestation. The subjects were recruited from 2003–2006 at two University Hospital locations in Nancy and Poitiers, France. Mothers and their children were excluded from participating in this investigation if the mothers were minors, carried multiplex, had gestational diabetes, illiteracy, or intention to give birth at a hospital that was not included in the study. Obstetric records, interviews, face-to-face or self-administered questionnaires, and clinical examinations were utilized for data collection. Clinical examinations included collecting biological samples, anthropometric and clinical examination measures at birth, one, three, and five years of age. Biological samples such as blood samples were utilized to conduct genotype testing for SNPs associated with obesity in adults. AR was analyzed via growth curves using separate mixed – effect cubic models for boys and girls.

The data from this investigation indicated that maternal and paternal BMI along with gestational weight gain and smoking during pregnancy were associated with EAR; 15.8 [ $\pm 3.1$ ] days per kg/m<sup>2</sup>,  $p = 1.9 \times 10^{-7}$ , -15.6 [ $\pm 3.9$ ] days per kg/m<sup>2</sup>,  $p = 5.6 \times 10^{-5}$ , -7.5 [ $\pm 2.9$ ] days per kg,  $p = 0.001$ , and -72.1 [ $\pm 32.6$ ] days,  $p = 0.03$  respectively. Birthweight z-score was the only offspring characteristic associated with EAR ( $P=.05$ ). Multiple factors in conjunction such as low birth weight of the offspring and excessive gestational weight gain of the mother during pregnancy increase the probability of EAR more than if those factors occurred individually in a pregnancy. The data also indicated that genetic susceptibility to obesity based on SNP alleles was also significantly associated with EAR in this

investigation. Thus, the authors conclude that genetic SNP markers for obesity along with perinatal factors such as paternal obesity, just stational weight gain, and a low birthweight are all early predictors or factors associated with EAR.

Jacota et. al (2017)<sup>23</sup> also utilized the Eden birth prospective cohort study for a data source for their investigation, although this research was published prior to the aforementioned investigation. In this investigation BMI of both the mothers and the children were calculated in addition to the average annual change before pregnancy as well as gestational weight gain for each woman. Z-scores were calculated of BMI at five years based on World Health Organization (WHO) sex standards. The study included 1069 children. Along with the other aforementioned methodologies that were followed as outlined previously, this research also highlighted that food questionnaires were sent to the mothers immediately after delivery for nutritional intake analysis in the last three months of pregnancy.

The data indicates that no association existed between maternal weight history and AR timing when maternal age and maternal education level were controlled for. BMI at AR tends to be lower in children were born of mothers that are of a lower weight than compared to mothers that are obese. Gestational weight gain was not significantly associated with EAR; gestational weight changes showed only weak correlation with children's BMI score = 0.08 P = 0.005, fat mass percent  $r = 0.08$  P = 0.009, and abdominal adiposity index  $r = 0.08$  P = 0.009. The multivariate model conducted by these researchers suggest a nonlinear positive relationship exist between a child's BMI score at the age of five and maternal pre-pregnancy BMI; children's BMI z-scores increased by an average of one standard deviation when maternal BMI increased from 15 to 22 kg/m<sup>2</sup>, there was no variation when maternal BMI ranged from 22-35 kg/m<sup>2</sup>. Class one obesity categorization of the mother or higher exhibited an even more pronounced increase in BMI z-score at the age of five for the offspring. The associations between maternal BMI and BMI z-score at the age of five remain significant when the multivariate analysis was adjusted to control for gestational weight gain. When maternal BMI and socioeconomic status were controlled for, gestational weight gain had significant associations with the offspring's BMI z-score at five years. The data suggests that adequate or insufficient weight gain during gestation was not associated with an increased BMI z-score at age five. The authors indicate that EAR and its associations with maternal BMI were attenuated in mothers that exhibited normal BMI pre-pregnancy. The authors indicate that pre-pregnancy weight loss prior to conception exhibited beneficial effects like those of normal weight women prior to pregnancy according to the data in this investigation.

Ip et. al (2017)<sup>10</sup> conducted a two-year longitudinal study in North Carolina with Latino Farm Workers and their children, ages 2.5-3.5 years, in order to evaluate dietary and physical activity patterns. All participants self-identified as Latino and only one child within the age range from each family could participate in this investigation; children with special needs were omitted from the data. This methodology utilized a sampling plan that was developed to recruit participants in specific locations such as those with programs including Head start in community health centers. Data collectors also conducted door-to-door recruitment in Latino neighborhoods. The participant, a parental figure, was interviewed at baseline and every three months for the entirety of the investigation. The interviews were conducted in Spanish typically in the participants home, or in another preferred location, from April 19, 2011 – July 30, 2014. The parental figures were offered \$10 for compensation for completing the interview process. Anthropometric data was measured on the children as well as physical activity at baseline, 3, 6, 9, 12, and 24 months of age. Nutritional intake was evaluated using 3-24 hour recalls during a seven-day period; this included one weekend and two weekdays. BMI was calculated and plotted for every observation; due to the age restraints of the subjects all EARs in this investigation were classified as early or very early. The researchers analyzed differences in AR timing in association with children's BMI and weight for age percentile at baseline, year one, and year two. The Waller – Duncan test was used for significant differences in continuous variables; the Pearson's chai square test was used beforehand. The Bonferroni adjustment pairwise comparisons were conducted by the researchers if the chi-squared result was significant.

The results of this investigation indicate that 86.3% of families completed the investigation who were invited to do so. Twenty children were excluded due to fewer than four BMI measurements which was not sufficient for calculations or analyzing associations appropriately. 18.2% of the children had a very early AR and 40% of the

children had early AR. 26.2% of participants were considered non-rebounders and 15.5% had non-classifiable growth curves for AR. The data suggest that a higher maternal BMI predicted EAR; a higher calorie intake also exhibited a similar association with EAR. The authors indicate that 1/3 of the children exhibit EAR before the age of five; maternal BMI appears to be the strongest indicator of EAR. It is important to note that the data also indicates that children with the highest levels of activity experienced AR one year later than their less active counterparts.

## Gestational Age

Franchetti et. al (2014)<sup>13</sup> conducted a longitudinal survey in Japanese newborns born January 10-17 or July 10-17 in 2001 whose parents responded to postal surveys sent by the government. Data was transcribed from the 21<sup>st</sup> century longitudinal survey in newborns conducted by the government in Japan. Data was collected at six months, 1.5, 2.5, 3.5, 4.5, and 5.5 years; this investigation utilized data ranging from 2001-2006. In total this investigation included 45,392 Japanese children; 23,608 boys and 21,784 girls. BMI is calculated using weight and height reports from parents who responded to all postal surveys. Gender specific cross-sectional distribution of BMI was calculated using the 25<sup>th</sup> median, 75<sup>th</sup>, 85<sup>th</sup>, 95<sup>th</sup>, and 99<sup>th</sup> percentile. However, BMI classifications were varied from standard to account for differences in obesity prevalence in Japan compared to other countries. AR timing was determined for each subject by creating a binary event a variable; survival analysis was performed using the Kaplan-Meier method including log-rank test for significance between groups. Cox proportional hazard models were used to estimate hazard ratios and GE models were used to investigate how specific factors affected BMI trajectories.

Data from this investigation indicated that 39.6% of obese children experienced EAR; as early as 4.5 years. These children exhibited a 48.5% higher hazard ratio for EAR incidence than non-obese children. The length of gestational period was the most important factor in the BMI at AR and AR timing. The authors conclude from this investigation that AR timing occurs earlier in children that exhibit obesity when compared to non-obese counterparts. Additionally, obese children exhibit a 50% increased risk of experiencing EAR by 4.5 years compared to non-obese children. The researchers indicate that the strongest association observed was between shorter gestational period and primary caretaker in association with AR timing.

Vereen et. al (2019)<sup>14</sup> was a unique respective longitudinal follow up investigation that included data on 501 preterm and 1423 full-term infants. These infants were born at three military health system hospitals in 2008: with either an Army, Navy, Air Force, Department of Defense, or US government affiliation. Anthropometric data from birth to discharge was transcribed for 175 of the children in total for this specific investigation; 115 full-term and 59 preterm children from birth to 8/9 years of age. Health records were utilized to extract weight and length data for children during the investigation period. Children with diagnosed medical conditions were excluded from subject to participation. AR was calculated for each subject using a second-degree polynomial regression of BMI on age; children had to have four or more data points from birth through 8/9 years of age to be included as well. T-test for independent samples compared preterm and non-preterm groups for age at AR; Pearson's coefficient was used to analyze correlations between factors, groups, and AR timing.

These United States, potentially foreign born due to military relation, children did not exhibit associations between gestational age and timing of AR. The data does indicate a negative association between age of AR and BMI z-score at 8-9 years;  $R = -.685$ . The data also suggested that a disassociation was exhibited for both full-term and preterm children;  $R = -.634$  and  $R = -.685$  respectively. Additionally, the data indicated an association between age at AR and weight at 8-9 years for both full-term and preterm infants. The data for full-term children suggest there was a significant negative association between age at AR and height at 8-9 years; Pearson  $r = 0.378$ ,  $p = 0.019$ ; there was no mention of this association in terms of preterm infants. The data suggest there are significant differences in BMI based on feeding method with a P value less than .001 when comparing formula feeding to BF. Preterm and non-preterm infants differed significantly in their weight z-scores with no effect by feeding method;  $P = .035$  and  $P = .000$  respectively. In summary, this investigation concluded that there is an association between the age at AR and growth at 8-9 years; an earlier AR is associated with a higher BMI at 8-9 years of age. However, there is no difference

between the age of AR when comparing preterm and full-term children. The authors articulated that rapid early catch-up growth is more strongly associated with EAR than gestational age. Nonetheless, children born less than 36 weeks of gestational age exhibited rapid weight gain in the first three months of life; this rapid weight gain is what is positively associated with elevated body fat percentages, waist circumference, total cholesterol, and low LDL cholesterol levels in early adulthood, not EAR.

Although some of the results from this investigation with a subject pool of United States citizens with military associations, may appear abnormal in comparison to results that are well established from investigations contributed to academic knowledge from other countries, we must always keep in mind the role of sociocultural factors in relation to morbidity incidence. Although the world is heading towards a more ethnically diverse base population, the United States has a unique representation of this phenomena currently. Individuals that participate in the various aspects of the United States military that may have families and offspring born in the military associated hospitals come from a plethora of ethnic and socioeconomic backgrounds due to the socio-economic advantages and social cultural honor that may be typically associated with serving in the United States defense organization in some manner. Typically, in research, participants are categorized in a way that does not appear to be communicated that they are multi-ethnic or of a mixed race; this important aspect of sociocultural information on the subject pool must either be ignored or communicated meticulously to accurately account for the general diversity of the population. Therefore, the results of this investigation were not completely in agreement with results from other countries such as Japan or Italy in terms of AR timing and gestational age.

Baldassare et. al (2020)<sup>24</sup> utilized data on children born in Bari, Italy at an intensive care unit at Aldo Moro University between 2008-2011. This prospective population-based study included children born in the NICU department of biomedical science and human oncology of Aldo Moro University in Bari, Italy that were not diagnosed with any conditions; along with the requirement to speak Italian and have a gestational age between 23-36 weeks. Data collection occurred at scheduled clinic visits at three, six, nine, 12, 15 and 24 months along with three, four, five, six, and seven years of age. Subjects were classified into groups corrected for birthweight according to gestational age, SGA, and LGA. The researchers utilize contingency tables in Chi squared analysis to evaluate associations between EAR and they are variables of interest. Multivariate regression models were created as well as students unpaired t-test to compare differences between children with and without EAR. Only 100 participants out of the original 411 subjects completed the entire investigation; the researchers discuss that due to the high incompleteness rate that statistical analysis of the data was not viable.

Despite statistical analysis limitations the data suggests that EAR was identified in 54% of preterm infants and in 30% in non-preterm infants. And association between EAR and gestational age was not observed through significance;  $p=.85$ . In this investigation BF duration and timing of introduction of other solid foods was also not significantly associated with EAR. However, the data does suggest that preterm infants that experience EAR also exhibited higher BMI than those that did not experience EAR ( $p=.021$ ). The authors discussed that EAR does elicit adverse health impacts in adulthood for children. Additionally, preterm birth may be considered a high-risk factor for EAR according to the data as premature infants that do exhibit EAR have higher BMI than those that do not.

## Infant Birth Weight

Joubert et. al (2013)<sup>25</sup> utilized data from a longitudinal study on Hungarian children born in 1980 through 1983. This data was transcribed from the Hungarian longitudinal growth study. This study only utilized a 2% sample size of the newborn population born between 1980-1983 and was conducted by the Hungarian central statistics office. Anthropometric data was collected at birth, every 30 days up to six months, every 60 days up to six to 12 months of age and quarterly until 24 months of age; annual examinations were performed 2-10 years of age and biannually from 10-18 years of age. 120 micro locations were utilized for data collection in the hospitals at birth - three years of age; measurements were conducted at educational institutions from the age of three for the duration of the data collection period. Parental self-reported questionnaires were utilized to gather information on lifestyle and nutritional habits before and

after birth as well as general health, education, and occupation status questions. BMI categories were used to assess subjects based on nutritional status; normal, overweight, and obese categories were created using age dependent BMI cut off points. T-test and ANOVA were used to analyze normally distributed variables in association with AR. Men Whitney test were used to evaluate associations with AR for abnormally distributed variables with two samples; the Kruskal– Wallis test was used for this analysis when comparing more than two samples. Chi squared analysis were used to determine homogeneity between subgroups and fitted curves were created to analyze adiposity peak, AR, and BMI at AR.

The data indicated that AR could be evaluated in 70% of the sample; AR could be estimated in 50% and in 20% error existed but could not be estimated. Small for gestational age and large for gestational age children had significantly higher AR when compared to average gestational age children. Small for gestational age children exhibited lower BMIs at AR when compared to large for gestational age children. Additionally, there was a high prevalence, about 10%, of absent AR; further investigations are required to validate the observations regarding a lack of AR. The researchers indicate that the higher the prenatal growth rate, SGA: AGA: LGA, the higher the body measurement parameters found at birth. Additionally, this phenomenon was observed with other factors; the higher the intrauterine growth rate the higher the BMI found after birth and at AR.

Maeyama et. al (2016)<sup>15</sup> conducted a longitudinal cohort study utilizing children born in Kobe Japan between 2006–2009. Children included in this investigation had records from birth to three years of age available for data transcription; 29,287 children born between 22 and 41 weeks of gestation were included in the study. Subjects were categorized into subgroups based on gestational age and BMI was calculated at four and nine months, and 1.5 and 3 years from data transcribed at the Kobe City Public Health Center. Analysis of the data was not conducted until April 1, 2015, after approval by the Planning and Coordination Bureau of the city of Kobe. Simple statistical calculations such as mean, standard deviation, median, range, or number/percentage was calculated for each group. Chi-squared test analysis and students t-test were also evaluated to analyze the data.

The data indicated that 1063, 3.6%, of children were small for gestational age. Children born small for gestational age or typically born before 34 weeks suggesting an association between gestational age and birth size. The mean height for a small for gestational age with 39 through 41 and 37 through 34 weeks of gestation increase with age. The mean height for SGA children with 34 through 36 weeks and less than 34 weeks of gestational age decreased at four months and then began to increase. The data also indicates that 91% of SGA children with 39 through 41 weeks of gestation caught up at four months of age; small for gestational age children with lower gestational ages how do you slower rate of catch-up growth. The data was able to identify AR in 7.1% of small for gestational age children; AR was not observed in children born less than 34 weeks however this specific data was not statistically significant as the sample size of children born in less than 34 weeks gestation was inadequate. The authors discuss that high trajectory during the first three years of life for small for gestational children is gestational age dependent. Additionally, the authors articulate that catch-up growth occurs faster in older GA children and decreases by subgroup. EAR was observed in SGA children less than 357 weeks as well greater than or equal to 34 weeks; EAR was not observed in gestation <34 weeks. It was also observed that small for gestational age children that were born less than 37 weeks of gestation exhibited significantly lower BMIs than their counterparts born equal to or greater than 37 weeks of gestation.

Shi et. al (2018)<sup>26</sup> conducted a longitudinal cohort study utilizing data from the growth and development of SGA's collected from 2004-2010 in Shanghai, China. The original longitudinal community-based cohort study included 32,370 SGA infants. Anonymous gestational age, birthweight, gender, and residential information was collected. Anthropometric measures were collected at birth and according to health protocol measures; this data was extracted from the Shanghai Center Disease Control Network. Anthropometric data collection occurred at birth, four months, eight months, one year, and two years; a follow-up measurement also occurred between 2 to 5 years. This investigation included 3000 for infants. WHO growth charts were used to calculate gender and age specific weight distributions to categorize subjects according to z-scores. Mixed effect regression models were used to determine the

one month through five-year BMI profiles for all of the week classes; age and BMI at AR was evaluated for each group.

The data indicates that there were differences in AR timing before the age of five between the different weight classes. This data highlights that for full term SGA infants, catch-up growth that is rapid and crosses to percentiles in the first several months of life that then attenuates to a maintenance rate of growth, that is on track, is the best model for decreasing adverse health outcomes. In this investigation EAR and higher BMI at AR was observed for growth classes one and two when compared to the other classes, however, there is an observable increase in the slopes of growth with increasing classes. The authors conclude that catch-up growth patterns may pose an increased risk of obesity for children later in life. The timing of AR and BMI at AR are influenced by the catch-up growth pattern experienced; class one and class two exhibited earlier and higher BMI at AR when compared to the other classes.

Lin et. al (2021)<sup>27</sup> utilized children born in the Minhand District of Shanghai, China from September 2010 – October 2013. This research transcribed data from a population based longitudinal study that included 13,616 children: 7,164 boys and 6,452 girls. The data was extracted from health records and included anthropometric data as well as other information documented in physician visits. Data on gestational factors and birth were transcribed from the birth records of the participants. BMI trajectories were created to determine the timing of AR; the researchers used age and BMI at AR in order to estimate timing of AR. The Wilson's rank sum test was used to detect factors that influence AR timing that would be considered continuous. Generalized linear models were used to identify upstream factors and risk ratios with 95% confidence intervals. Gestational and early life factors were analyzed for associations with AR timing using Univariable regression analysis. It is important to note that the researchers both articulate and defend the appropriateness of a P value of <.25 as significant in this investigation. Additionally, multivariable regression was done in the forward stepwise manner including variables identified in the univariable analysis as significant.

Of the 13,616 children included in the investigation, 10,985 children had estimates of AR calculated based on their extracted data. The data suggest that sex, preterm birth, low birth weight, SGA, multiple pregnancies, and sleep duration greater than 17 hours a day for the first three months along with greater than 14 hours a day four to 11 months indicated significant influences on AR timing. Additionally, the data suggests that advanced maternal age greater than 35 years, SGA, and a BF duration shorter than 4–6 months were associated with EAR in the multivariate model. The data indicated that offspring that were breastfed longer than four months exhibited a decreased risk of EAR compared to their counterparts who were not breast-fed or were breast-fed a duration shorter than four months; adjusted RR = 0.80, 95% CI: 0.73–0.87,  $p < 0.001$ . Additionally, offspring of mothers of advanced maternal age along with children born SGA exhibited an increased risk of EAR; Adjusted RR = 1.21, 95% CI: 1.07–1.36,  $p < 0.01$  and adjusted RR = 1.20, 95% CI: 1.04–1.39,  $p = 0.01$  respectively. Ultimately the authors conclude that the timing of AR was associated or influenced by multiple factors; sex, preterm birth, BF duration, advanced maternal age, and/or SGA. It is important to note that in this investigation positive associations between AR and BF were not observed for breast-feeding durations longer than six months; this may ease the burden of mothers who attempt to breastfeed for 12 months or longer until the child is able to completely be nourished through food. Due to the results of this investigation more studies are needed to investigate the effects between BF duration and the timing of AR to further uncover if extending the breast-feeding duration elicits further attenuation of morbidity development later in life. The authors highlight that the factors investigated in this investigation were all modifiable and should therefore be used to develop interventions to postpone AR.

## Strengths and Limitations

Research publications were widely available for the factors discussed in this narrative review. Pertinent article identification was limited as to not overwhelm the reader with too many sources. Publications were particularly abundant investigating BF in association with AR as well as maternal BMI. Publications were available from various regions of the globe allowing for a global analysis of the relationships between AR timing and the investigated factors.



This narrative review originally aimed to analyze maternal diet quality and gestational exercise in relation to AR and AR timing. However, studies investigating these factors in relation to AR were not identified through thorough investigations of online databases. This indicates that further extensive research is critical to evaluate the association between AR and maternal diet quality and/or gestational exercise. These investigations may be feasible in a randomized controlled trial investigation without committing ethics violations and would greatly add to the scientific body of knowledge.

## Conclusions

Despite rigorous research there appears to be no best way to manipulate factors to beneficially influence AR timing. Investigations for the factors, BF, maternal BMI, infant gestational age, and infant birth weight, exhibited mixed results. Investigations typically identify the association that having a healthy BMI prior to pregnancy has beneficial impact on AR timing. From the perspective of the researcher these mixed results are highly influenced by ethnicity and geographical location. Geographical locations in which racial homogeneity is uncommon, such as the U.S., indicate weaker associations between the factors and AR timing. It is the conclusion of the researcher that it is best to consider the ethnic and geographical location of the individual when deciding what factors may most influence AR timing of the infant. Therefore, decisions on maximizing the health and delaying AR timing of the infant must occur in an individualized setting between the mother and/or parents and healthcare provider.

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